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Identification of those most likely to benefit from a low-glycaemic index dietary intervention in pregnancy

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Abstract

The present study is a secondary analysis of the ROLO study, a randomised control trial of a low-glycaemic index (GI) diet in pregnancy to prevent the recurrence of fetal macrosomia. The objectives of the present study were to identify which women are most likely to respond to a low-GI dietary intervention in pregnancy with respect to three outcome measures: birth weight; maternal glucose intolerance; gestational weight gain (GWG). In early pregnancy, 372 women had their mid-upper arm circumference recorded and BMI calculated. Concentrations of glucose, insulin and leptin were measured in early pregnancy and at 28 weeks. At delivery, infant birth weight was recorded and fetal glucose, C-peptide and leptin concentrations were measured in the cord blood. Women who benefited in terms of infant birth weight were shorter, with a lower education level. Those who maintained weight gain within the GWG guidelines were less overweight in both their first and second pregnancies, with no difference being observed in maternal height. Women who at 28 weeks of gestation developed glucose intolerance, despite the low-GI diet, had a higher BMI and higher glucose concentrations in early pregnancy with more insulin resistance. They also had significantly higher-interval pregnancy weight gain. For each analysis, women who responded to the intervention had lower leptin concentrations in early pregnancy than those who did not. These findings suggest that the maternal metabolic environment in early pregnancy is important in determining later risks of excessive weight gain and metabolic disturbance, whereas birth weight is mediated more by genetic factors. It highlights key areas, which warrant further interrogation before future pregnancy intervention studies, in particular, maternal education level and inter-pregnancy weight gain.

Key words: Diet in pregnancy: Birth weight: Macrosomia: Glycaemic index: Glucose intolerance

Rates of intra-uterine growth, particularly whether restrictive or excessive, can have profound and lasting implications for later adult health[1,2]. In particular, the large-for-gestational age fetus is predisposed to a variety of adverse obstetric and neonatal outcomes[3,4] and in the long term, infants that are at the highest end of the distribution for weight or BMI are more likely to be obese in childhood, adolescence and early adulthood than other infants[5,6]. Glucose is the main fuel for intra-uterine growth[7]. Carbohydrates are classified according to their induced glycaemic response as either high or low glycaemic index (GI)[8]. In recent years, interest has been increasing in the role of the GI in pregnancy, and in particular its potential to modulate fetal growth[9,10].

We have recently reported the results of the ROLO study, a randomised control trial of a low-GI diet in pregnancy to prevent the recurrence of fetal macrosomia[11]. It was the first low-GI dietary intervention study to be carried out in pregnant women who previously delivered a macrosomic infant, and the largest randomised control trial of a low-GI diet in pregnancy.

Approximately 50 % of all women in the ROLO study went on to have a macrosomic infant in their second pregnancy, and there was no significant difference in mean infant birth weight between the groups (our primary outcome).

We did find that an introduction of a low-GI diet in pregnancy significantly reduced gestational weight gain (GWG) (our secondary outcome). By 40 weeks of gestation, women in the dietary intervention arm had gained 1·5 kg less than those who received no dietary intervention. A significant proportion of women in each arm of the study exceeded the GWG guidelines, as outlined by the Institute of Medicine (IOM)[12]. However, women who received the low-GI diet were significantly less likely to exceed these GWG guidelines, with just 37·7 % doing so compared with 47·9 % of women in the control arm. Our intervention did not include specific weight gain advice for women in the intervention group.

Abbreviations: GI, glycaemic index; GWG, gestational weight gain; HOMA, homeostasis model assessment; IOM, Institute of Medicine.

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Additionally, we found that the use of a low-GI dietary intervention in pregnancy reduced the incidence of maternal glucose intolerance at 28 weeks of gestation. A significantly higher proportion of women in the control arm at 28 weeks had either a fasting glucose concentration of >5·1 mmol/l or a glucose challenge test result of >7·8 mmol/l.

These findings imply that a once-off dietary education session in pregnancy is beneficial in terms of maternal outcomes, though not in terms of fetal or neonatal outcomes. The ROLO study population comprises a large, well-characterised cohort with uniform, standardised and longitudinal assessments of maternal and fetal size, as well as maternal and fetal insulin resistance and metabolism. Further interrogation of this cohort of pregnant women may not only reveal why some women did respond to the intervention and others did not, but also allow for the characterisation of a particular maternal phenotype that is likely to find this form of intervention particularly useful, and as such, may guide future research in this important area.

The primary objective of the present study was to identify which women, in terms of phenotypic and biochemical characteristics, are most likely to respond to a low-GI dietary intervention in pregnancy to reduce the recurrence of fetal macrosomia, in an attempt to identify from early pregnancy those who might benefit.

Its secondary objective was to identify which characteristics are associated with improvements in maternal glucose homeostasis and GWG.

Experimental methods

The present study is a secondary analysis of all women from the intervention arm of the ROLO study, a randomised control trial. A detailed methodology of the ROLO study has been published previously[11,13].

Patient selection

In brief, women were recruited at their first antenatal consultation at 13·8 (SD 2·4) weeks. Subjects were excluded if they had any underlying medical conditions, were <18 years of age, had previous gestational or pre-existing type 1 or type 2 diabetes or were unable to give full informed consent.

Ethical approval

Ethical approval was granted by the National Maternity Hospital Ethics Committee (2007).

Data collection and trial management

At their first antenatal visit, all patients had their weight and height recorded and their BMI calculated. Concentrations of fasting blood glucose, insulin and leptin were measured and a mid-upper arm circumference recorded. Questions relating to maternal lifestyle habits, including physical activity, smoking, breast-feeding practices and education level, were included in the FFQ and given to the subjects at their first antenatal visit. Maternal education level was used as a surrogate marker of socio-economic status. Education level was categorised as one of six categories: 6, complete third level (higher-level degree); 5, some third level (certificate/diploma); 4, complete second level; 3, some second level; 2, primary education only; 1, no education.

Maternal weight was recorded at each antenatal consultation and total GWG calculated according to the IOM guidelines[12]. At 28 weeks of gestation, repeat fasting blood glucose, insulin and leptin concentrations were measured and glucose challenge testing 1 h after a 50 g glucose load was carried out. At delivery, infant birth weight, length and head circumferences were recorded, and a cord blood sample for analysis of fetal glucose, leptin and C-peptide concentrations was taken. The present controlled trial was registered as ISRCTN54392969.

Dietary intervention

The intervention comprised one dietary education session lasting 2 h in groups of two to six women with a research dietitian. The mean gestational age of those attending the dietary session was 15·7 (SD 3·0) weeks.

The education session focused on the GI. Women were encouraged to choose as many low-GI foods as possible and to exchange high-GI carbohydrates for low-GI alternatives. Women received written resources about low-GI foods after the education session. The recommended low-GI diet was euenergetic, and women were not advised to reduce their total energy intake.

Dietary assessment

All subjects completed a 3 d food diary during each trimester of pregnancy where the type and amount of all foods and beverages consumed were recorded over three consecutive days. Subjects were encouraged to include 1 weekend day during the recording period. Subjects were instructed to quantify their food consumed using either the manufacturer's weight on the food packaging or standard household measures. Dietary data were entered into WISP version 3.0 (Tinuviel Software). The 3 d food diary was used to assess the dietary GI of each patient and the response to the dietary intervention.

Laboratory methods

Multianalyte profiling was performed on the Luminex Magpix system (Luminex Corporation). Plasma concentrations of leptin, insulin and C-peptide were determined by the Human Endocrine Panel. Maternal insulin resistance was calculated using the homeostasis model assessment (HOMA) index[14]:

$$\text{HOMA score} = (\text{fasting insulin } (\mu\text{U/ml}) \times \text{fasting glucose (mmol/l)})/22.5.$$

Fetal insulin resistance was assessed by cord blood C-peptide estimation.

Statistical analysis

Maternal demographic characteristics in early pregnancy, details from the previous pregnancy notes and maternal glucose and insulin assessments were compared using Student's *t* test, Mann–Whitney *U* test and χ^2 test for the following groups:

(1) Those who did and those who did not have a recurrence of fetal macrosomia.
(2) Those who did and those who did not exceed the GWG guidelines as outlined by the IOM.
(3) Those who did and those who did not have impaired glucose tolerance in later pregnancy.

Recurrence of fetal macrosomia was assessed as an infant birth weight of ≥4000 g in the second pregnancy. Impaired glucose tolerance was diagnosed when women had either a fasting glucose concentration of ≥5·1 mmol/l or a glucose challenge test of >7·8 mmol/l at 28 weeks of gestation.

Results

A total of 372 women in early pregnancy from the intervention arm of the ROLO study were included in the secondary analysis. Compared with the control group, maternal GI was significantly reduced in the intervention group at the second and third trimesters (56·1 (SD 4) *v.* 57·8 (SD 4), $P<0·001$ and 56 (SD 3·7) *v.* 57·7 (SD 3·9), $P<0·001$, respectively).

Comparison of the maternal characteristics of those who did and those who did not have a recurrence of fetal macrosomia following the low-glycaemic index dietary advice in pregnancy

Overall, fetal macrosomia (birth weight ≥4000 g) recurred in 50·8 % (*n* 189/372) of women who received the low-GI dietary advice in pregnancy. A comparison of the maternal characteristics of those 189 women and 183 women who delivered their second infants weighing <4000 g is outlined in Table 1.

During the first pregnancy, no difference was observed between the two groups in terms of first birth weight or GWG.

In the second pregnancy, there was no difference observed between the two groups in terms of mean maternal BMI in early pregnancy (27·12 (SD 5·2) *v.* 26·36 (SD 5·1) kg/m^2, $P=0·1$); however, women who went on to deliver a second macrosomic infant were found to be heavier (75·5 (SD 14·0) *v.* 71·8 (SD 14·8) kg, $P=0·02$) and taller (167·1 (SD 6·1) *v.* 165·2 (SD 6·7) cm, $P=0·01$). They also had higher mid-upper arm circumferences (29·9 (SD 3·8) *v.* 29·1 (SD 4·1) cm, $P=0·04$), a marker of maternal adiposity.

No difference was observed between those who did and those who did not go on to deliver a second macrosomic infant in terms of maternal fasting glucose concentrations or insulin resistance (HOMA) in early pregnancy, though a significant difference in leptin concentrations was observed during early pregnancy (Table 1).

Interestingly, maternal education level did differ between the two groups, with a higher mean education level in those who went on to deliver a second macrosomic infant (4·4 (SD 2·1) *v.* 3·9 (SD 2·4), $P=0·03$).

Comparison of the maternal characteristics of those who did and those who did not exceed the gestational weight gain guidelines as outlined by the Institute of Medicine following the low-glycaemic index dietary advice in pregnancy

A comparison of the maternal characteristics of those who did and those who did not exceed the GWG guidelines as outlined by the IOM is contained in Table 2.

Table 1. Comparison of the maternal characteristics of those who did and those who did not have a recurrence of fetal macrosomia following the low-glycaemic index dietary advice in pregnancy*

(Mean values and standard deviations for normally distributed data; median values and interquartile ranges for non-parametric data (homeostasis model assessment (HOMA) index and leptin concentration))

	Macrosomia recurrence (*n* 189)		No macrosomia recurrence (*n* 183)		
	Mean	SD	Mean	SD	*P*
BMI in the first pregnancy (kg/m^2)	25·66	4·5	25·87	4·6	0·7
Gestational weight gain in the first pregnancy (kg)	15·0	5·2	14·7	5·1	0·7
Birth weight in the first pregnancy (g)	4269	268	4236	254	0·2
BMI in the current pregnancy (kg/m^2)	27·12	5·2	26·36	5·0	0·1
Height (cm)	167·1	6·1	165·4	6·7	0·01
Arm circumference (cm)	29·89	3·8	29·12	4·1	0·04
Fasting glucose concentration in early pregnancy (mmol/l)	4·49	0·3	4·40	0·3	0·2
HOMA index in early pregnancy†					0·2
Median	2·24		2·09		
Interquartile range	1·17–3·3		1·9–3·3		
Leptin concentration in early pregnancy (pg/ml)					0·005
Median	15 093		11 236		
Interquartile range	8419–23 674		6866–20 841		
Education level‡	4·42	2·1	3·9	2·4	0·03

* Independent Student's *t* test used for parametric data and Mann–Whitney *U* test used for non-parametric data.
† HOMA = (fasting insulin (μU/ml) × fasting glucose (mmol/l))/22·5.
‡ Education level was categorised as one of six categories: 6, complete third level (higher-level degree); 5, some third level (certificate/diploma); 4, complete second level; 3, some second level; 2, primary education only; 1, no education.

Women who exceeded the GWG guidelines in their second pregnancies following the low-GI dietary intervention were heavier at the beginning of their first pregnancies (76·01 (SD 13·8) *v.* 69·8 (SD 13·2) kg, $P=0·001$), and also had higher GWG during that pregnancy (17·5 (SD 4·5) *v.* 12·9 (SD 4·8) kg, $P<0·001$).

Their early pregnancy BMI were higher in the index pregnancy (28·3 (SD 5·1) *v.* 26·2 (SD 5·4) kg/m^2, $P<0·01$), with no difference being observed in maternal height. They also had more adiposity with larger mid-upper arm circumferences (30·5 (SD 3·8) *v.* 29·2 (SD 3·7) cm, $P=0·005$). There was no difference observed between those who did and those who did not exceed the GWG guidelines following the low-GI dietary intervention in terms of maternal fasting glucose concentrations or insulin resistance (HOMA) in early pregnancy, though serum leptin concentrations were found to be higher in those who exceeded the GWG guidelines during early pregnancy (Table 2).

Comparison of the maternal characteristics of those who did and those who did not have impaired glucose tolerance following the low-glycaemic index dietary advice in pregnancy

A comparison of the maternal characteristics of those who did and those who did not have impaired glucose tolerance following the low-GI dietary intervention in pregnancy is outlined in Table 3.

At 28 weeks of gestation, women who had either a fasting glucose concentration of >5·1 mmol/l or a glucose challenge test result of >7·8 mmol/l had higher BMI in early pregnancy than those who did not (27·9 (SD 4·9) *v.* 26·1 (SD 4·5) kg/m^2, $P=0·005$). However, there was no difference in BMI between the two groups in their first pregnancies (25·4 (SD 4·1) *v.* 25·6 (SD 4·5) kg/m^2, $P=0·7$), with those who developed glucose intolerance having significantly increasing BMI between pregnancies (25·4 (SD 4·1) *v.* 27·9 (SD 4·9) kg/m^2, $P=0·008$).

They also had significantly higher fasting glucose concentrations in early pregnancy (4·51 (SD 0·3) *v.* 4·42 (SD 0·3), $P=0·05$) with more insulin resistance and higher leptin concentrations than those who did not go on to develop glucose intolerance in later pregnancy. However, there was no difference in education level between those who did and those who did not develop glucose intolerance following the low-GI dietary intervention in pregnancy.

Discussion

The present secondary analysis of a cohort of pregnant women from the intervention arm of the ROLO study has defined the maternal characteristics in early pregnancy associated with a response to a low-GI dietary intervention in pregnancy with respect to three important parameters of obstetric risk: infant birth weight; maternal glucose metabolism; GWG.

We found that women who went on to deliver a second macrosomic infant were taller with a higher mean education level. Women who exceeded the GWG guidelines were found to be heavier in both their first and second pregnancies, though no difference was observed in maternal height. They also had more adiposity with larger mid-upper arm circumferences. At 28 weeks of gestation, women who developed glucose intolerance had a higher BMI with significantly higher fasting glucose concentrations in early pregnancy with more insulin resistance. For each analysis (birth weight, weight gain and glucose intolerance), women who responded to the low-GI dietary intervention had lower fasting leptin concentrations in early pregnancy than those who did not.

Table 2. Comparison of the maternal characteristics of those who did and those who did not exceed the gestational weight gain (GWG) guidelines following the low-glycaemic index dietary advice in pregnancy*

(Mean values and standard deviations for normally distributed data; median values and interquartile ranges for non-parametric data (homeostasis model assessment (HOMA) index and leptin concentration))

	Exceeded GWG guidelines (*n* 139)		Did not exceed GWG guidelines (*n* 229)		
	Mean	SD	Mean	SD	*P*
BMI in the first pregnancy (kg/m^2)	28·27	5·1	26·18	5·4	0·01
GWG in the first pregnancy (kg)	17·5	4·4	12·9	4·8	0·001
Birth weight in the first pregnancy (g)	4254	273	4243	254	0·9
BMI in the current pregnancy (kg/m^2)	27·27	5·1	26·18	5·4	0·01
Height (cm)	166·9	6·7	165·7	6·1	0·1
Arm circumference (cm)	30·48	3·8	29·19	3·7	0·005
Fasting glucose concentration in early pregnancy (mmol/l)	4·49	0·3	4·42	0·3	0·1
HOMA index in early pregnancy†					0·8
Median	2·23		2·11		
Interquartile range	1·13–3·48		1·14–3·48		
Leptin concentration in early pregnancy (pg/ml)					0·0
Median	15 670		10 956		
Interquartile range	9689–25 308		6524–19 348		
Education level‡	4·11	2·1	4·2	2·3	0·7

* Independent Student's *t* test used for parametric data and Mann–Whitney *U* test used for non-parametric data.
† HOMA = (fasting insulin (μU/ml) × fasting glucose (mmol/l))/22·5.
‡ Education level was categorised as one of six categories: 6, complete third level (higher-level degree); 5, some third level (certificate/diploma); 4, complete second level; 3, some second level; 2, primary education only; 1, no education.

Table 3. Comparison of the maternal characteristics of those who did and those who did not have impaired glucose tolerance following the low-glycaemic index dietary advice in pregnancy*

(Mean values and standard deviations for normally distributed data; median values and interquartile ranges for non-parametric data (homeostasis model assessment (HOMA) index and leptin concentration))

	Glucose intolerance (*n* 21)		No glucose intolerance (*n* 351)		
	Mean	SD	Mean	SD	*P*
BMI in the first pregnancy (kg/m^2)	25·4	4·1	25·6	4·5	0·7
Gestational weight gain in the first pregnancy (kg)	15·5	4·4	14·9	5·3	0·6
Birth weight in the first pregnancy (g)	4245	226	4265	280	0·6
BMI in the current pregnancy (kg/m^2)	27·84	4·9	26·12	4·5	0·005
Height (cm)	164·3	5·8	166·7	6·5	0·004
Arm circumference (cm)	29·88	358	29·21	3·7	0·13
Fasting glucose concentration in early pregnancy (mmol/l)	4·51	0·3	4·42	0·3	0·05
HOMA index in early pregnancy†					0·02
Median	2·42		2·11		
Interquartile range	1·34–4·36		1·06–3·35		
Leptin concentration in early pregnancy (pg/ml)					0·04
Median	14 555		13 096		
Interquartile range	8264–25 032		7204–21 663		
Education level‡	4·25	2·1	4·34	2·3	0·7

* Independent Student's *t* test used for parametric data and Mann–Whitney *U* used for non-parametric data.
† HOMA = (fasting insulin (μU/ml) × fasting glucose (mmol/l))/22·5.
‡ Education level was categorised as one of six categories: 6, complete third level (higher-level degree); 5, some third level (certificate/diploma); 4, complete second level; 3, some second level; 2, primary education only; 1, no education.

Primary analysis of this cohort demonstrated no difference in the recurrence of fetal macrosomia following the commencement of a low-GI diet in pregnancy. However, the diet was associated with a significant improvement in maternal outcomes, with less GWG and less glucose intolerance.

Interestingly, the findings of the present secondary analysis revealed a similar disparity between maternal and fetal outcomes. There was no difference between those who did and those who did not go on to deliver a second macrosomic infant in terms of maternal BMI in early pregnancy, though mothers who were taller were more likely to deliver a second infant weighing >4000 g. In contrast, maternal BMI was significantly higher in women who went on to exceed the GWG guidelines as outlined by the IOM and in those who developed glucose intolerance at 28 weeks of gestation. Similarly, there was no difference between those who did and those who did not go on to deliver a second macrosomic infant in terms of maternal fasting glucose concentrations, insulin resistance (HOMA indices) or leptin concentrations in early pregnancy; however, those who developed glucose intolerance had significantly higher fasting glucose concentrations in early pregnancy with more insulin resistance (higher HOMA indices) and higher leptin concentrations than those who did not.

These findings confirm that the maternal metabolic environment in early pregnancy is important in determining later risks of excessive weight gain and metabolic disturbance. In contrast, infant birth weight in this healthy, non-diabetic population is mediated to a greater extent by genetic factors, such as maternal height.

Notably, maternal leptin concentration in early pregnancy was the single marker that differed consistently in each of the three analyses of the present study. Despite low-GI dietary advice, women who gave birth to second macrosomic infants, exceeded the GWG guidelines or developed glucose intolerance in later pregnancy all had significantly higher leptin concentrations in early pregnancy than those who did not. There raises an interesting possibility that perhaps maternal leptin concentration is a more sensitive marker than maternal BMI, adiposity or, indeed, insulin resistance of an underlying predisposition towards pregnancy complications in such a cohort of women.

The present findings in relation to maternal education level, a surrogate marker of socio-economic status, are interesting. Again, we observed a maternal/fetal disparity, with education level being associated with the recurrence risk of fetal macrosomia, but not with maternal weight gain or glucose homeostasis. These findings would suggest that women with lower education levels are perhaps more likely to respond to dietary education in pregnancy. Perhaps this group is more susceptible to aberrant fetal growth secondary to poor dietary choices, and should be considered as a group likely to respond to simple dietary education measures. These findings highlight the public health importance of education during pregnancy about healthy lifestyle choices.

Similarly, our findings in relation to the effect of interval pregnancy weight gain and glucose intolerance are important for public health education. We found that women who developed glucose intolerance in their second pregnancies had significantly increased their BMI from the first to second pregnancy (from a mean of 25 kg/m^2 to just under 29 kg/m^2). This highlights the important role of post-partum weight retention and, indeed, weight gain in dictating future metabolic risk, for both the mother and the baby. It would suggest that obstetricians and carers should advise all women, including those with

a normal BMI, of the potential hazards of interval pregnancy weight gain for future pregnancies.

There are a number of potential limitations to these data that warrant further consideration. The present study is a subgroup analysis and therefore likely to be underpowered to draw concrete conclusions. This analysis was performed with the intention of further interrogation of the ROLO study data to further our understanding of why some women did and some did not respond to the dietary intervention; as such, multiple comparisons were made which raised the possibility of type 1 statistical error.

In addition, infant birth weight alone is a relatively crude, if clinically applicable, assessment of intra-uterine growth. Follow-up assessment of neonatal and childhood adiposity, currently in progress, will add invaluable data to separate physiological from pathological fetal growth.

These findings have important implications for clinical practice. They suggest a particular maternal phenotype that is likely to respond, or not, to low-GI dietary intervention in pregnancy. Importantly, we identified no harm associated with the introduction of a low-GI diet in pregnancy. These findings may allow for tailoring of dietary intervention based on maternal characteristics in early pregnancy, such as early pregnancy weight and glucose, in order to improve outcomes in all maternal phenotypes. Perhaps a more intensive regimen, with more regular feedback and re-enforcement, may be necessary for those who fit certain criteria at first antenatal consultation. A recent publication by Rhodes *et al.*[15] reported the results of a pilot study comparing a low-glycaemic load diet with a low-fat diet in a group of forty-six overweight and obese pregnant women. These authors employed a much more intensive regimen including weekly reinforcement and home food delivery. Their results in this particular patient group reflect our experience with little or no effect on infant birth weight but an improvement in maternal outcomes. Perhaps a once-off dietary education session could be considered for all women at risk of excessive gestation weight gain or impaired glucose tolerance, with a more intensive regimen employed for overweight and obese women in early pregnancy.

The benefits of an intervention that reduces maternal GWG, irrespective of maternal BMI, cannot be underestimated. Maternal weight gain during pregnancy has been reported to be independently linked to adverse obstetric outcomes for all BMI categories[3,4]. There are also potential maternal implications to excessive GWG, such as an increased operative delivery rate, a higher likelihood of post-partum weight retention and a predisposition to later obesity[16,17]. Similarly, there is a clear association between maternal hyperglycaemic, even at levels below those diagnostic of gestational diabetes, and a variety of adverse maternal, fetal and neonatal outcomes[18].

Further work is still necessary to determine whether pregnancy interventions can reduce the recurrence of fetal macrosomia in euglycaemic women. It is clear from our work that a low-GI diet alone is not sufficient to combat the problem, despite conferring maternal benefits.

The present secondary analysis has confirmed that infant birth weight is a complex interplay between genetic and environmental factors. There was no difference between those who did and those who did not go on to deliver a second macrosomic infant in terms of maternal BMI in early pregnancy, though mothers who were taller with higher education levels were more likely to deliver a second infant weighing >4000 g. There was also no difference between those who did and those who did not go on to deliver a second macrosomic infant in terms of maternal fasting glucose concentrations, insulin resistance or leptin concentrations in early pregnancy. This would suggest that in this cohort of women, at least, genetic factors played a more significant role in the recurrence risk of fetal macrosomia than did the maternal environment and metabolic milieu. This may be at least in part explained by the strict inclusion criteria of the ROLO study. This group of study mothers was specifically selected to allow us to examine the effect of a low-GI diet among healthy euglycaemic women. Perhaps our selection criteria introduced a degree of selection bias towards women who are giving birth to larger babies due to genetic potential rather than due to aberrations in maternal metabolism.

In conclusion, there are no adverse outcomes associated with the use of a low-GI diet in pregnancy. There are potential benefits, in particular in terms of limiting maternal GWG to within the IOM guidelines, and an improvement in maternal glucose homeostasis. These findings were identified following a single, formal small-group dietetic session in early pregnancy in the ROLO study. This suggests that this type of simple dietary intervention is adequate in improving maternal nutrition in a general population of women.

The present analysis would suggest that modifications of this pregnancy intervention may be necessary in order to optimise outcomes for women at the higher end of the spectrum in terms of weight, adiposity and insulin resistance in order to improve these important benefits for all.

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The authors' contributions were as follows: F. M. M. conceived and designed the study; G. C. assisted with the data collection; R. M. M. and M. E. F. contributed to the study design, data collection and manuscript preparation; J. M. W. carried out the analysis and wrote the manuscript. All the authors reviewed and revised the final version of the manuscript.

None of the authors has any conflict of interest to declare.

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